Applicants have claimed the benefit of the filing date of French priority application No 95 08069, filed April 7, 1995. A verified English translation of this priority application was previously filed in copending Application No. 08/671,757 on January 18, 2001. Applicants have subsequently become aware that the selective underlining of nucleic acid sequences identified as SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:4, and SEQ ID NO:5, was not correctly translated from the French application when this verified translated copy was made. The underlining of the nucleic acid sequences referred to above is correct and conforms to that in FR 95 08069, in a new verified translation of the French priority application, which was filed in copending Application No. 08/671,757 on August 16, 2001. The amendments being made to the specification at pages 3 and 18 are being made so that the instant application conforms to FR 95 08069.

The meaning of the underlining of selected nucleotides in SEQ ID NO:1 (OLF1bA-1) and SEQ ID NO:2 (OLF1bA-2) is explained in the portion of Example 1 appearing at page 14, line 6 to page 15, line 8. This Example describes an experiment to isolate a homologue of the LcrD/FlbA gene family from *H. pylori*. Relying on the fact that "homologues of the LcrD/FlbA family . . . possess very conserved domains," the inventors "use[d] two of these conserved regions (MPGKQM, amino acids 151 to 156 of the LcrD protein of *Yersinia*) and MDGAMKF (amino acids 189 to 195 of LcrD) for defining two degenerate oligonucleotides (OLF1bA-1 [SEQ ID NO:1] and OLF1bA-2 [SEQ ID NO:2])." (Application at page 14, lines 21-28). The conserved amino acid sequences on which SEQ ID NO:1 (OLF1bA-1) and SEQ ID NO:2 (OLF1bA-2) are based are underlined in Figure 3. (Application at page 12, lines 25-28; Figure 3).

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A comparison of the sequences of OLF1bA-1 (SEQ ID NO:1) and OLF1bA-2 (SEQ ID NO:2) with the underlined amino acids in Figure 3 makes clear that the underlined nucleotides correspond to the third nucleotide "wobble positions" present in the various codons encoding a single amino acid. This is shown below for OLF1bA-1 (SEQ ID NO:1).

ATG	CCTCGA	GGTCGA	AAAG	CAAG	ATG
Met	Pro	Gly	Lys	Gln	Met

This "built in" degeneracy increases the likelihood that a homologue will be amplified.

Also enclosed and being filed herewith are computer readable and hard copy versions of a replacement sequence listing. In the previously filed sequence listing, the degenerate positions within SEQ ID NO:1 and SEQ ID NO:2 were not correctly identified. This problem has been corrected in the enclosed replacement sequence listing.

The meaning of the selective underlining of OLF1bA-7 (SEQ ID NO:4) and OLF1bA-8 (SEQ ID NO:5), at page 6, and in Table 1, at page 18, as amended herein, is explained in the application at page 16, lines 23-26. Each of these oligonucleotides contains a *Bam*H1 restriction site at its 5' end. (Application at page 16, lines 25-26). In both OLF1bA-7 (SEQ ID NO:4) and OLF1bA-8 (SEQ ID NO:5), the *Bam*H1 restriction site, GGATCC, occurs at positions 3-8, and is underlined. As indicated in Table 1, at page 18, the 3' portions of these oligonucleotides were designed to hybridize to positions 515-534 and 2092-2111 of *FlbA*, respectively.

Applicants submit that, as described above, no new matter is added by these amendments to the specification.

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Amendments to the Claims

With entry of this Preliminary Amendment claims 31-36 and 43-57, 59, and 61-65 are pending in this application. Claims 31-36, 45-46, 51-52, and 57(b)-(e) have been withdrawn as drawn to a non-elected invention.

Support for the amendments to claims 43-44 and 49-50, and for new claims 62-65, is found in the specification at page 7, lines 3-18. This section teaches that the invention is directed towards "bacterial strains of *Helicobacter pylori* which possess an aflagellate phenotype." (Application at page 7, ll 3-5). This aflagellate phenotype is defined as resulting from "the mutation, by substitution, addition, and/or deletion of bases or of a nucleotide fragment, of the above-defined nucleotide sequence of the *flbA* gene," such that the mutant strain "no longer expresses the FlaA and FlaB proteins." (Application at page 7, lines 6-8, lines 13-14) (claims 43 and 49). In one embodiment, the bacterial strain additionally "no longer expresses the proteins of the sheath." (Application at page 7, lines 14-15) (claims 62 and 64). Additional strains of the invention "lack the hook protein." (Application at page 7, lines 16-18) (claims 44, 50, 63, and 65).

Support for the amendments to claims 55, 56, and 59 is found at page 7, lines 14-15 and page 8, lines 20-35.

In Paper No. 14, the Examiner withdrew newly submitted claims 45-46, 51-52, and 57(b)-(e) from further consideration as drawn to a non-elected invention, pursuant to 37 C.F.R 1.142(b). The basis for this determination was the characterization of the originally elected invention (an election made with traverse in Paper No. 7) as drawn to *flbA* mutants, and the allegation that claims 45-46, 51-52, and 57 (b)-(e) are drawn to *H. pylori* mutants "which express *flbA* (non *flbA* mutants)." (Paper No. 14, at 3). Applicants

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submit that this reading of the claims is incorrect. The claims in question depend from independent claims 43 and 49. Claims 43 and 49 read on methods utilizing *H. pylori* bacterial strains "having an aflagellate phenotype resulting from a mutation in the *flbA* gene," such that the mutant strain "no longer expresses the FlaA and FlaB proteins." Claims 45-46 and 51-52, as they depend from claims 43 and 49, respectively, add the additional limitations that "the *H. pylori* bacterial strain is obtained from strain N6," (claims 45 and 51) or that "the aflagellate strain of *H. pylori* is strain N6flbA" (claims 46 and 52). Properly read, claims 45-46 and 51-52 must be understood as reading on aflagellate *flbA* mutant strains of *H. pylori*. Thus, claims 45-46 and 51-52 are not directed to H. pylori mutants "which express *flbA* (non *flbA* mutants)," and should be properly considered as directed to the same elected invention as claims 43-44, 47-50, 53-56, and 58-61.

Because claims 45 and 46 each defines a subgenus within the broader genus of claim 43, and claims 51 and 52 likewise each defines a subgenus within the broader genus of claim 49, the examination of claims 45-46 and 51-52 would not require any additional search. The search already undertaken for the broader genus claims necessarily also encompassed the subject matter of the subgenus claims. For the foregoing reasons, applicants request that the restriction requirement for claims 45-46 and 51-52 be withdrawn.

Applicants courteously request that this amendment be entered and kindly request the Examination of this application. If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

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Respectfully submitted,

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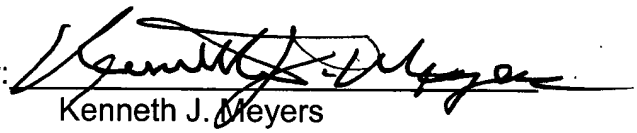
Dated: August 23, 2001

By: 
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Appendix

Amendments to the Specification[3]:

The paragraph running from Page 2, line 35 to Page 3, line 7 (amended):

The invention therefore relates to a nucleotide sequence from the *flbA* gene regulating the biosynthesis of the proteins of the *Helicobacter pylori* flagella, characterized in that it is able to hybridize, under conditions of high stringency, with a probe corresponding to a nucleotide fragment from *H. pylori* which has been amplified using two oligonucleotides having the following sequences:

OLF1bA-1: [ATGCCTCGAGGTCGAAAAGCAAGATG]

ATGCCTCGAGGTCGAAAAGCAAGATG (SEQ ID NO:1).

OLF1bA-2: [GAAATCTTCATACTGGCAGCTCCAGTC]

GAAATCTTCATACTGGCAGCTCCAGTC (SEQ ID NO:2), or able to hybridize, under conditions of high stringency, with these oligonucleotides.

The paragraph beginning at Page 3, line 8 (amended):

Such a sequence can be obtained by the steps of:

- screening a genomic library containing the chromosomal DNA of an *H. pylori* strain with a probe corresponding to a nucleotide fragment from *H. pylori* which has been amplified using two oligonucleotides having the following sequences:

OLF1bA-1: [ATGCCTCGAGGTCGAAAAGCAAGATG]

ATGCCTCGAGGTCGAAAAGCAAGATG (SEQ ID NO:1).

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3 Text that is removed by the amendments is enclosed in brackets; text that is added is in bold face type.

OLF1bA-2: [GAAATCTTCATACTGGCAGCTCCAGTC]

GAAATCTTCATACTGGCAGCTCCAGTC (SEQ ID NO:2), or able to hybridize, under conditions of high stringency, with these oligonucleotides,

- recovering the DNA sequences, which hybridize with said probe,

- subcloning the DNA sequences, which have been obtained in an appropriate vector of the plasmid type and selecting those modified vectors, which hybridize[,] under conditions of high stringency[,] with the probe corresponding to the DNA fragment from *H. pylori* which has been amplified using oligonucleotides OLF1bA-1 and OLF1bA-2,

- sequencing the DNA fragments contained in the plasmid vectors which hybridize with the above mentioned probe, and determining the open reading frame contained in these fragments.

Page 18, Table 1, (amended):

Table 1: Oligonucleotides employed in this study

Oligo-nucleotide	Position	Strand	Nucleotide Sequence
OLF1bA-1	AS 151-156 (LcrD)	+	[ATGCCTCGAGGTCGAAAAGCAAGATG] (SEQ ID NO:1) **ATGCCTCGAGGTCGAAAAGCAAGATG**
OLF1bA-2	AS 189-195 (LcrD)	-	[GAAATCTTCATACTGGCAGCTCCAGTC] (SEQ ID NO:2) **GAAATCTTCATACTGGCAGCTCCAGTC**
OLF1bA-7	515-534	+	[CGGGATCCGTGGTTACTAATGGTTCTAC] (SEQ ID NO:4) **CGGGATCCGTGGTTACTAATGGTTCTAC**
OLF1bA-8	2092-2111	-	[CGGGATCCTCATGGCCTCTTCAGAGACC] (SEQ ID NO:5) **CGGGATCCTCATGGCCTCTTCAGAGACC**

Amendments to the Claims[4]:

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4 Text that is removed by the amendments is enclosed in brackets; text that is added is in bold face type.

43. (Amended) A method for the *in vitro* detection of [an infection due to] **antibodies against** *H. pylori* in a sample of biological fluid from a patient, wherein the method comprises:

a) bringing the sample into contact with an *H. pylori* bacterial strain having an aflagellate phenotype resulting from a mutation in the *flbA* gene of said *H. pylori* bacterial strain**, wherein said *flbA* mutant *H. pylori* bacterial strain no longer expresses** [such that either the *flbA* gene is no longer expressed in the *H. pylori* bacterial strain, or the expression of the *flbA* gene in the *H. pylori* bacterial strain does not enable] the [A and B flagellins] **FlaA and FlaB proteins** [or the sheath that contains them to be biosynthesized and, if this is the case, does not enable the *H. pylori* anchoring protein or the hook to be synthesized]; and

b) detecting an immunological reaction between the bacterial strain and antibodies directed against *H. pylori* and which are present in the sample.

44. (Amended) The method as claimed in claim 43, wherein the [aflagellate] ***flbA* mutant** *H. pylori* strain also does not express the hook protein **(or anchoring protein) of the flagellum** of *H. pylori.*

49. (Amended) **A** [M]**m**ethod for the *in vitro* detection of [an infection due to] **antibodies against** *H. pylori* in a sample of biological fluid from a patient, wherein the method comprises:

a) bringing the sample into contact with a bacterial extract from an *H. pylori* bacterial strain having an aflagellate phenotype resulting from a mutation in the

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flbA gene of said *H. pylori* bacterial strain, **wherein, said *flbA* mutant *H. pylori* bacterial strain no longer expresses** [such that either the *flbA* gene is no longer expressed in the *H. pylori* bacterial strain, or the expression of the *flbA* gene in the *H. pylori* bacterial strain does not enable] the [A and B flagellins] **FlaA and FlaB proteins** [or the sheath that contains them to be biosynthesized and, if this is the case, does not enable the *H. pylori* anchoring protein or the hook to be synthesized]; and

b) detecting an immunological reaction between the bacterial strain and antibodies directed against *H. pylori* and which are present in the sample.

50. (Amended) The method as claimed in claim 49, wherein the [aflagellate] ***flbA* mutant** *H. pylori* strain also does not express the hook protein **(or anchoring protein) of the flagellum** of *H. pylori.*

55. (Amended) The method as claimed in claim 49, wherein the bacterial extract is a total bacterial extract [of an aflagellate strain of *H. pylori*].

56. (Amended) The method as claimed in claim 49, wherein the bacterial extract is a n-octyl glucoside extract [of strain N6*flbA*- having deposit Accession No. NCIMB 40747].

59. (Amended) The method [according to claim 57] **as claimed in claim 49**, wherein the bacterial extract is obtained after extracting with PBS or glycine.

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